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PATENT

## REMARKS

Claims 78-81, 93-102 and 106 are pending in the present application. Claims 78-81, 93-102, and 106 have been amended herein. New claims 117-181 have been added herein. Upon entry of the present Amendment, claims 78-81, 93-102, 106, and 117-181 will be pending.

The claims have been amended to replace the term "double-stranded RNA substrate enzyme" with the term "composition." Because at least portions of the first and second oligonucleotides are base-paired with one another, at least portions of the composition are double-stranded. The claims have not been narrowed because of this amendment.

Claims 78, 94-96 and 98-101 have been amended to recite that the first and second oligonucleotides each comprise from eight to fifty nucleoside subunits. No new matter has been added.

New claims 117-181 have been added herein, support for which can be found at, for example, page 7, lines 8-16; page 8, lines 4-14; page 22, lines 6-23; and page 24, lines 5-27 of the specification.

Applicant thanks the Examiner for the opportunity to interview the present application on July 12, 2004, at which time the claims and the references or record were generally discussed.

**I. The Claimed Embodiments Are Novel**

Claims 96, 98, 99 and 100 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 5,013,830 (hereinafter, the "Ohtsuka reference"). Applicant traverses the rejection and respectfully requests reconsideration of the same in view of the amended claims.

The Office alleges that the Ohtsuka reference discloses double stranded oligonucleotides in which the RNA portions serve as modifications that increases the affinity of an oligonucleotide and in which the 2'-O-Me modifications increase resistance to nucleases. The interpretation by the Office that the RNA portion serves as a modification that increases the affinity, however, is not consistent with the definition of a chemical modification set forth in Applicant's specification. Indeed, Applicant's specification makes quite clear that the oligomeric compounds can be RNA, DNA, or both. Thus, a chemical modification would be a modification

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of the DNA or RNA itself -- the Office's assertion that a change in an oligonucleotide from "all DNA" to "RNA/DNA" represents a "chemical modification" does not conform to the meaning given to the term "chemical modification" in the specification, and, indeed, to the meaning used in the art. Nonetheless, Applicant has amended claims 96, 98, 99 and 100 to recite "at least one of said first and said second oligonucleotides having a further portion that includes a chemical modification that increases the affinity of said oligonucleotide for the other oligonucleotide," support for which can be found, for example, on page 7 of the application as filed. The Ohtsuka reference fails to teach or suggest that the first and second oligonucleotides comprise from eight to fifty nucleoside subunits. Table 5 of the Ohtsuka reference, specifically cited by the Examiner, sets forth several oligonucleotide pairs. At least member of the pairs is a representation of oligonucleotide "XV", discussed, for example, in columns 5, 7, and 9-10 as "a high molecular weight RNAWS-S(+) (90mer; compound XV)..." and is clearly outside the range from eight to fifty nucleoside subunits.

As the Ohtsuka reference fails to teach or even suggest that the first and second oligonucleotides comprise from eight to fifty nucleoside subunits, the Ohtsuka reference fails to anticipate claims 98, 99 and 100. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §102(b) be withdrawn.

Claims 78, 94, 95, 99 and 101 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 5,256,775 (hereinafter, the "Froehler reference"). Applicant traverses the rejection and respectfully requests reconsideration of the same in view of the amended claims.

The Office alleges that the because Froehler reference reports oligonucleotides that are 3-50 nucleotides in length and contain modifications on the 3' and 5' ends to protect from nucleases (referring to column 5, for example) which can be used to hybridize and inhibit an RNA target such as mRNA (referring to column 1 and 12, for example), the instantly claimed invention has been disclosed. Claims 78, 94, 95, 99 and 101, however, have been amended to recite that the first and second oligonucleotides comprise from eight to fifty nucleoside subunits, support for which can be found, for example, on page 7 of the application as filed. The Froehler

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reference fails to teach or suggest that the first and second oligonucleotides comprise from eight to fifty nucleoside subunits. As set forth by the Office, columns 1 and 12 of the Froehler reference indicate that the oligonucleotides of Froehler "block protein synthesis by hydrogen bonding to complementary messenger RNA." The second "oligonucleotide" (i.e., messenger RNA) reported in the Froehler reference, however, does not comprise "from eight to fifty nucleotides," as recited in amended claims 78, 94, 95, 99 and 101.

As the Froehler reference fails to teach or even suggest that the first and second oligonucleotides comprise from eight to fifty nucleoside subunits, the Froehler reference fails to anticipate claims 78, 94, 95, 99 and 101. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §102(b) be withdrawn.

**II. The Claims Are Definite**

Claims 78-81, 93-102 and 106 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Office asserts that the specification does not provide a definition of the term "a double stranded RNA substrate." Although Applicant disagrees and notes that the term would be readily understood by the art-skilled, the claims have been amended to delete this term, rendering the rejection moot. In view of the foregoing, Applicant respectfully requests that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

**III. The Specification Provides Written Description Support for the Claims**

Claims 78-81, 93-102 and 106 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Office alleges that the term "double stranded RNA substrate" was "not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Although Applicant's specification, as filed, provides several exemplary double stranded RNases (including, for example, human dsRNase from T-24 cells, *E. coli* RNase III, and a yeast dsRNase; *see*, pages 5-6 of the specification) such that the skilled artisan would readily appreciate that Applicant was in possession of the claimed invention, solely in an attempt to advance the prosecution of the present application to

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allowance, Applicant has amended the claims to delete the phrase "double stranded RNA substrate", thus rendering the present rejection moot. In view of the foregoing, Applicant respectfully requests that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

**IV. Conclusion**

Applicant believes the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicant invites the Examiner to contact the undersigned at (215) 665-6904 to clarify any unresolved issues raised by this response.

Respectfully submitted,



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